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EDITORIAL

Disseminated Intravascular Coagulation: New Bottles For An Old Wine

SCARCELY A CLINICAL JOURNAL is published, nowadays, without an article or two ascribing some fresh disorder to inadvertent intravascular coagulation. The appealing view that many apparently diverse pathologic processes have a common basis in diffuse thrombosis within small blood vessels has a lusty champion in McKay, whose review appears elsewhere in this issue.

Like all new ideas, the concept that disseminated intravascular coagulation is an important pathologic process has its origins in the distant past. As early as 1834, de Blainville[1] demonstrated that the intravenous injection of brain tissue led immediately to lethal, massive intravascular clotting. A half century later, Woolridge[2] observed that animals would survive if the infusion of tissue extract was sufficiently slow; indeed, no gross intravascular clots could be found. For some time after the infusion, the animals' blood was incoagulable, and further infusions of tissue extracts were harmless. Mills[3] and others showed that the blood in such animals would not clot because it was depleted of fibrinogen. In modern terms, the tissues used in these various experiments furnished tissue thromboplastin which activated the extrinsic pathway of thrombin formation and, in this way, initiated clotting within the animals' blood stream. In agreement with this view, clotting factors other than fibrinogen have been found to be depleted (or "consumed") after the infusion of tissue extracts. Antihemophilic factor (Factor VIII),[4] proaccelerin (Factor V),[5] prothrombin (Factor II)[5] and platelets[6] disappear most rapidly, changes resembling those which take place when blood clots in a test tube. In addition, deficiencies of Christmas factor (Factor IX), Stuart factor (Factor X) and Factor VII may be detected.[7] At the same time, the plasma acquires inhibitory activity retarding the formation of a fibrin clot[8] and, inconstantly, fibrinolytic activity. Defibrination can also be brought about by the injection of thrombin[9] or certain snake venoms.[10]

In animals subjected to sublethal infusions of clot-promoting agents, few if any thrombi are found, even under the microscope. Two hypotheses have been proposed to explain this paradox. Perhaps the clots which form are promptly lysed by plasmin. This fibrinolytic enzyme is activated from its precursor, plasminogen, with particular facility if fibrin is present.[11] Were this true, the blood stream should contain degradation products of the digested fibrin. These products could readily account for the concomitant retarded formation of fibrin for, in the test tube, they inhibit the action of thrombin and interfere with the polymerization of fibrin.[12,13] Alternatively, the formation of fibrin initiated by the infusion of procoagulant substances might be incomplete. Conceivably, the first products of clotting, monomeric units of fibrin, perhaps polymerized with fibrinogen itself, might be readily removed from the blood stream before they had a chance to form macroscopic clots.[14,15] In support of this, material resembling fibrin has been found in reticuloendothelial cells after the infusion of clot-promoting agents. Of course, these hypotheses are not mutually exclusive, nor can one be certain that the fibrin ingested by macrophages has not already been lysed by plasmin.

Two clinical syndromes have been delineated